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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/850,128	05/08/2001	Robert H. Getzenberg	076333/0238	1058

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EXAMINER
EPPS, JANET L

ART UNIT	PAPER NUMBER
1635	6

DATE MAILED: 05/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/850,128	Applicant(s) GETZENBERG, ROBERT H.	
	Examiner Janet Epps	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-15,18-20,22,23,25-31,33-39 and 44-49* is/are pending in the application.

4a) Of the above claim(s) *4-14,18-20,23,30,31,35-39 and 44-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,22,25-29,33,34,48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

2. Claims 15, 22, 25-29, and 33-34 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the Official Action mailed 8-15-01.

Applicant's arguments filed 11-08-01 have been fully considered but they are not persuasive. Applicants traverse the instant rejection by way of amending the claims to recite particular renal matrix proteins, and have further defined the proteins by means of a range of isoelectric point and a range of molecular weight. Moreover, Applicants argue that they have fulfilled the written description requirement as to the claimed subject matter by describing the claimed invention in sufficient detail so that one skilled in the art can clearly conclude that [he] "the inventor invented the claimed invention."

However, contrary to Applicant's assertions, it remains that the specification as filed does not provide a sufficient written description of the claimed invention. The instant now amended reaclaims read on an antibody which binds a nuclear matrix protein, or a fragment thereof, that is present in normal renal cells but absent in cancerous renal cells, or that is absent in normal renal cells but present in cancerous renal cells. The claimed invention reads on a genus of antibodies targeted to a broad genus of nuclear matrix proteins and fragments thereof. The polypeptides,

which bind the claimed antibodies of the present invention, encompass all corresponding proteins from other species, mutated forms, allelic variants, splice variants, and so forth. Additionally, the antibodies of the present invention include those that are capable of binding to fragments of the renal matrix proteins of the present invention, wherein said fragment encompass isolated fragments, and fragments of the claimed proteins embedded within another protein. The specification provides insufficient written description to support the genus of antibodies encompassed by the instant claims. Other than a range of iso-electric points (pI; for example, "about 9.30"), and range of molecular weights (for example, "about 53 kD"), the instant claims do not recite any particular structural amino acid sequence information that may be associated with the genus of polypeptides encompassed by the claimed invention.

3. Claims 29, and 33-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims read on a method of treating a cell proliferative disorder associated with a renal matrix protein selected from the group consisting of RCCA-1, RCCA-2, RCCA-3, RCCA-4, RCCA-5, and RCNL-1 comprising administering an effective amount of an antibody, which blocks or enhances the function of said renal matrix protein.

First it is noted that Applicants have not provided any examples wherein they have isolated monoclonal or polyclonal antibodies targeting the renal matrix proteins of the present invention, wherein Applicants demonstrated that said antibodies were capable of blocking or enhancing the function of said renal matrix protein. There is no doubt that it is within the

available knowledge of one of skill in the art to isolate antibodies targeting the renal matrix proteins of the present invention, however one of skill in the art would further have to determine, *de novo*, whether the isolated antibody is capable of blocking or enhancing the function of the renal matrix protein that it binds to.

Furthermore, the specification contemplates treating a cell proliferative disorder comprising administration of an antibody that binds to a nuclear matrix protein, or a fragment thereof, of the present invention to a patient. However, the specification as filed does not provide sufficient guidance or instruction that would enable one of skill in the art to use the claimed compositions throughout the full scope of the claimed invention without undue experimentation. The specification teaches that the nuclear matrix proteins of the present invention are present in normal renal cells but absent in cancerous renal cells, or absent in normal renal cells but present in cancerous renal cells. Applicants have not demonstrated that they are in possession of inhibitory antibodies which block the activity of a nuclear matrix protein, or of stimulatory antibodies which enhance the activity of a nuclear matrix protein. Moreover, Applicants clearly have not provided any nexus between the expression patterns of the nuclear matrix proteins (NMPs) and the therapeutic efficacy administering an antibody targeting the NMPs of the present invention.

It is not feasible to extrapolate the teachings of the specification to the instant claims since it is well known that the art of cancer therapy is highly unpredictable. For example, Gura (Science, 1997, Vol. 278, pp. 1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have

shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second paragraph). In addition, Hartwell et al. (Science, 1997, Vol. 278, pp. 1064-1068) teach that an effective chemotherapeutic must selectively kill tumor cells, however most effective anticancer drugs have been discovered by serendipity and that the exact molecular alterations that provide selective tumor cell killing are unknown and that even understanding the detailed molecular mechanism by which a drug acts often provides little insight into why the treated tumor cell dies (bridging paragraph 1064-1065). Due to the known unpredictability of the cancer therapy art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the antibodies of the present invention can be used in a method of treating a cell proliferative disorder associated with a renal matrix protein.

Moreover, in view of the teachings of Hartwell and Gura, as discussed above, it appears that anti-tumor agents must accomplish several tasks in order to be effective. These agents must be delivered into the circulation that supplies the tumor or metastatic cells and interact at the proper site of action, at a sufficient concentration and for a sufficient period of time. The specification as filed does not teach one of skill in the art how to deliver the claimed compositions to a particular target tissue within an organism in order to produce the desired therapeutic result, i.e. treating a cell proliferative disorder. In addition, variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The claimed antibodies may be inactivated *in vivo* before producing a sufficient effect, for example by degradation, immunological activation or due to an inherently short half-life. The specification does not provide sufficient guidance or instruction in regard to

these issues and provides no working examples that would allow one skilled in the art to use the claimed antibodies throughout the full scope of the claims without undue experimentation.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 22, 25-28, and 48-49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-4, and 15 of U.S. Patent No. 6,232,443. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the issued US Patent and those of the instant application recite a method for detecting a cell proliferative disorder in a subject, comprising contacting a cellular component from a subject with a reagent that binds to a cellular component associated with a nuclear matrix protein, wherein said reagent is an antibody, the cellular component is a

protein taken from the subject's kidney. The claims of the issued US Patent obviously overlap in scope with the claims of the present invention. The claims of the instant invention differ from the claims of the issued Patent to the extent that the claims also encompass the use of antibodies that bind fragments of the nuclear matrix proteins of the present invention. However, one of ordinary skill in the art would recognize that antibodies targeting the full protein, would also potentially bind a fragment corresponding to the same epitope that the antibody recognizes in the full protein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Friday 8:30AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L Epps, Ph.D.
Examiner
Art Unit 1635

JLE
May 1, 2002

SEAN McGARRY
PRIMARY EXAMINER